PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

SUN PHARMACEUTICAL INDUSTRIES LIMITED,
SHRIVASTAVA Ratnesh
Acme Plaza
Andheri East, Andheri Kurla Road,
400059 Mumbai
India

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing
(day/month/year) 30 August 2004 (30.08.2004)

Applicant's or agent's file reference
MTX_102

REPLY DUE
within 2 months/~~days~~ from
the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IN 2003/000294	2 September 2003 (02.09.2003)	2 September 2002 (02.09.2002)

International Patent Classification (IPC) or both national classification and IPC
IPC[7]: A61K 31/421, 9/14, 45/06

Applicant
SUN PHARMACEUTICAL INDUSTRIES LIMITED

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I.	☒	Basis of the opinion
II.	☐	Priority
III.	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV.	☐	Lack of unity of invention
V.	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI.	☒	Certain documents cited
VII.	☒	Certain defects in the international application
VIII.	☐	Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 02.01.2005.

Name and mailing address of the IPEA/AT	Authorized officer
Austrian Patent Office Dresdner Straße 87, A-1200 Vienna	KRENN M.
Facsimile No. 1/53424/200	Telephone No. 1/53424/435

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International application No.
PCT/IN 2003/000294

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:
pages , as originally filed
pages , filed with the demand
pages , filed with the letter of

☐ the claims:
pages , as originally filed
pages , as amended (together with any statement) under Article 19
pages , filed with the demand
pages , filed with the letter of

☐ the drawings:
pages , as originally filed
pages , filed with the demand
pages , filed with the letter of

☐ the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , filed with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages

☐ the claims, Nos.

☐ the drawings, sheets/fig

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as „originally filed".*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 19-22,25,26.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 19-22,25,26 are so unclear that no meaningful opinion could be formed *(specify)*:

Characterization of pharmaceutical dosage forms by their modes of administration is insufficient; thus claims 19-22 resp. the dependent claims 25 and 26 were not considered in establishing the present examination.

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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V. **Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	8-14	YES
	Claims	1-7,15-18,23,24	NO
Inventive step (IS)	Claims	----	YES
	Claims	1-18,23,24	NO
Industrial applicability (IA)	Claims	1-18,23,24	YES
	Claims	----	NO

Citations and explanations

The following documents have been cited in the Search Report:

D1: US 4036957 A
D2: WO 02/45693 A1
D3: DE 10153078 A1
D4: US 6407128 B1

By referring to a pharmaceutical preparation comprising acetylsalicylic acid, metaxalone and opt. a dispersing (= solubilizing) agent or a wetting agent, wherein the components of said (micronized) preparation provide a particle size < 0.07 mm, D1 anticipates claims 1-7, 15-17,23 and 24.

D2 pertains to a micronized active agent, e.g. metaxalone providing a preferred particle size from less than 100µm, which is uniformly dispersed in a matrix composed of one or more excipients selected from the group of fatty alcohol, triglyceride, partial glyceride and fatty acid ester, which might act as solubilizing agents. Such pharmaceutical preparations represent compositions with enhanced oral bioavailability; thus D2 anticipates claims 1-7 and 15-18.
Although D2 does not refer to metaxalone providing either the specific surface area or the particle size distribution described in the present application, inventiveness of claims 1-18 is not given, because D2 describes a particle size of metaxalone up to 1-20µm, which are inevitably associated with a elevated surface area per unit volume.

As none of the cited documents explicitly refers to the details described in claims 8-14, said claims show novelty.

After filing of the priority document D3 is not anymore considered to be a relevant document.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Box V (page 1)

D4 is regarded as state of the art, because it does not disclose a solubility-improved form, but a recommendation to administer metaxalone together with food.

Industrial applicability is given

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VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
DE 10153078 A1	22.5.2003	30.10.2001	

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

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VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The characterizing parts of claims 1,2,5 and 8 were not considered in establishing the present report, because they include insufficiently defined formulations, namely "..pharmaceutical composition has enhanced oral bioavailability." (claims 1,8), "..a pharmaceutically acceptable solubility-improved form." (claim 2) and "..high-energy crystalline form of metaxalone." (claim 5).